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10/549,317	09/16/2005	Kenji Soejima	081356-0247	8219

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EXAMINER	
HADDAD, MAHER M	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/549,317	SOEJIMA ET AL.	
	Examiner	Art Unit	
	Maher M. Haddad	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12/4/07*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-14* is/are pending in the application.

4a) Of the above claim(s) *5-7 and 14* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4 and 8-13* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *09/05; 09/06&08/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 1-14 are pending.

2. Applicant's election without traverse of Group I, claims 1-4 and 8-13 directed to a polypeptide comprising a neutralizing epitope region in von Willebrand factor-specific cleaving protease (hereinafter, also referred to as vWFCP or ADAMTS-13), which is recognized by an antibody against the protease, or a peptide fragment derived from the polypeptide and a composition thereof, filed on 12/4/07, is acknowledged.

3. Claims 5-7 and 14 are withdrawn from further consideration by the Examiner, 37 C.F.R. § 1.142(b) as being drawn to nonelected inventions.

4. Claims 1-4 and 8-13 are under examination as they read on a polypeptide comprising a neutralizing epitope region in von Willebrand factor-specific cleaving protease (hereinafter, also referred to as vWFCP or ADAMTS-13), which is recognized by an antibody against the protease, or a peptide fragment derived from the polypeptide and a composition thereof.

5. Applicant's IDS, filed 09/16/05, 09/21/06 and 08/21/07, is acknowledged, however, the International Search Report of PCT/US0004/003602 (A2) was crossed out but the references listed thereon had been considered. Further, the JP-10500705 A (A1) was crossed out because the English translation of the document was not found.

6. Claim 11 is objected to under 37 CFR 1.75(c), as being of improper dependent form because a multiple dependent claim cannot depend from two sets of claims drawn to different features.

7. Claims 11-12 are objected to under 37 CFR § 1.75(c) as being in improper form because a multiple dependent claim cannot depend from any other multiple dependent claim. See MPEP § 608.01(n). Even though these claims are in improper form, the examiner has chosen to examine claims.

8. For clarity and the precision of the language, it is suggest that the phrase "such as" in the claim 11 be change to "wherein the modification comprises".

9. The specification is objected to because "**X**688X" on page 11, 4¶ is misspelled, the correct spelling is "**W**688X". Correction is required.

10. 35 U.S.C. § 101 reads as follows:

"Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter or any new and useful improvement thereof, may obtain a patent therefore, subject to the conditions and requirements of this title".

11. Claims 1-4 are rejected under 35 USC 101 because the claimed invention is directed to non-statutory subject matter.

Claims 1-4, as written, do not sufficiently distinguish over proteins as they exist naturally because the claims do not particularly point out any non-naturally occurring differences between the claimed products and the naturally occurring products. In the absence of the hand of man, the naturally occurring products are considered non-statutory subject matter. *See Diamond v. Chakrabarty*, 447 U.S. 303, 206 USPQ 193 (1980). The claims should be amended to indicate the hand of the inventor, e.g., by insertion of "Isolated" or "Purified". See MPEP 2105.

12. The following is a quotation of the second paragraph of 35 U.S.C. 112.

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

13. Claims 4 and 8-13 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A. The transitional phrase "consisting of" in claim 4 excludes any element or ingredient not specified in the claim. "Consisting of" defined as closing the claim to the inclusion of materials other than those recited except for impurities ordinarily associated therewith (see MPEP 2111.03). However, claim 4 further recites that one or several amino acids are deleted, substituted, or added, or a peptide fragment derived from the polypeptide. Given claim 4 closed the language on the polypeptide, it is not clear how the specific polypeptide of aa449-687 of SEQ ID NO: 1 would include the recited modifications.

B. The recitation "peptide fragment derived from the polypeptide composed of a polypeptide" recited in claim 11 is indefinite. It is not clear how the original polypeptide differ from the derived peptide composed of polypeptide. It is not clear how the smaller peptide would compose a larger polypeptide.

14. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

15. Claims 1-4 and 8-13 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated polypeptide of SEQ ID NO: 1, an isolated polypeptide consisting of amino acids 446-687 of SEQ ID NO: 1 and a composition thereof, does not reasonably provide enablement for a polypeptide "comprising" any neutralizing epitope region in vWF-cp/ADAMTS-13 which is recognized by an antibody against the protease, or any

peptide derived from the polypeptide in claim 1, or the polypeptide or the peptide fragment "derived from" said polypeptide, wherein the neutralizing epitope region is located in a region from position 449-687 in an amino acid sequence shown in SEQ ID NO: 1, in claim 2, or a polypeptide "comprising" an amino acid sequence from position 449-687 in an amino acid sequence shown in SEQ ID NO:1, or any peptide fragment "derived from" the polypeptide in claim 3, a polypeptide comprising an amino acid sequence consisting of an amino acid sequence from position 449-687 in an amino acid sequence shown in SEQ ID NO: 1. "where one of several amino acids are deleted, substituted, or added, the polypeptide being recognized by an antibody against vWF-cp, or a peptide fragment derived from the polypeptide" in claim 4, or a reagent for antibody measurement comprising a polypeptide "having a complete sequence composing ADAMTS-13, or a polypeptide or a peptide fragment derived from the polypeptide in claim 8, where in an autoantibody in a TTP patient is an object to be detected in claim 9; or a "pharmaceutical" composition for treating a patient positive for an anti-ADAMTS-13 antibody comprising, as an active ingredient, a polypeptide or a peptide fragment derived from the polypeptide in claim 10, or the pharmaceutical composition for treating a patient positive for an anti-ADAMTS-13 antibody, wherein the pharmaceutical composition comprises, as an active ingredient, a polypeptide or a peptide fragment derived from the polypeptide composed of a polypeptide or a polypeptide according to claims 1-4, which lacks reactivity with an anti-ADAMTS-13 antibody by modification such as molecular substitution, deletion or insertion in claim 11, wherein the pharmaceutical composition is administered to the patient to thereby neutralize the antibody in claim 12, or a composition comprising a ligand specific to an anti-ADAMTS-13 antibody for treating a patient positive for an anti-ANDAMTS-13 antibody, comprising , as an active ingredient, a polypeptide or a peptide fragment derived from the polypeptide according to claim s1-4, which is bound with a carrier and brought into contact with plasma from the patient to be used for removing the anti-ADAMT fragment antibody from the plasma from the patient in claim 13. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The specification disclosure does not enable one skilled in the art to practice the invention without an undue amount of experimentation.

Factors to be considered in determining whether undue experimentation is required to practice the claimed invention are summarized *In re Wands* (858 F2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)). The factors most relevant to this rejection are the scope of the claim, the amount of direction or guidance provided, the lack of sufficient working examples, the unpredictability in the art and the amount of experimentation required to enable one of skill in the art to practice the claimed invention.

The specification discloses the full-length and truncated ADAMTS-13 polypeptides, Full 1427, T1135X, W1016X, W897X, W808X, W746X, W688X, T581X, Q449X, W387X and P285X). However, the specification discloses that only the autoantibody show reactivity with a region up to the W688X and a region at the Q449X show no reactivity with all of the antibody fractions form three patients, a region from a Cys-rich region to a spacer region which is between Q449X-

W688X (see Examples 1 and 2 in particular).

Besides the full-length polypeptide and the polypeptides that comprises the Cys-rich/spacer region, the specification fails to discloses polypeptides comprising any neutralizing epitope or any fragment derived from the 449-687 region of SEQ ID NO:1. Neither is antibody binding seen as sufficiently limiting since an antibody epitope may be as small as 6-15 shared amino acid residues (e.g., Lerner Nature 1982; 299:592-596, see page 595-596) and places no limitations on the function of the protein containing the polypeptide sequence recognized.

Further, since the claimed polypeptide are used as a reagent for antibody measurement, then any change in the polypeptide of SEQ ID NO: 1 and fragments thereof would affect the binding specificity of the antibody. Colman *et al* in Research in Immunology (145(1):33-36, 1994) teach single amino acid changes in an antigen can effectively abolish antibody antigen binding. Abaza *et al* in Journal of Protein Chemistry (11(5):433-444, 1992) teach that single amino acid substitutions outside the antigenic site on a protein effect antibody binding. Futher, Lederman *et al* in Molecular Immunology (28:1171-1181, 1991) disclose that a single amino acid substitution in a common allele ablates binding of a monoclonal antibody (see entire document). Additionally, Li *et al* in PNAS (77:3211-3214, 1980) disclose that dissociation of immunoreactivity from other biological activities when constructing analogs (see entire document).

Because of this lack of guidance, an undue experimentation would be required to determine which modifications would be acceptable to retain occluding structural and functional activity, and the fact that the relationship between the sequence of a protein/peptide and its tertiary structure (i.e. its activity) are not well understood and are not predictable, it would require an undue amount of experimentation for one of skill in the art to arrive at the claimed modifications, fragments, peptides or neutralizing epitope region of SEQ ID NO:1 encompassed by the claimed invention.

Also, at issue is whether or not the claimed composition would function as pharmaceutical composition. In view of the absence of a specific and detailed description in Applicant's specification of how to effectively use the pharmaceutical composition as claimed, and absence of working examples providing evidence which is reasonably predictive that the claimed pharmaceutical composition are effective for in vivo use, and the lack of predictability in the art at the time the invention was made, an undue amount of experimentation would be required to practice the claimed pharmaceutical composition with a reasonable expectation of success.

The lack of any working examples is exacerbated because the invention is in a highly unpredictable art-treat a patient positive of anti-ADAMTS-13 antibody- and while the level of skill of in the art may be high, the state of the prior art is that it is in fact unknown and untested what are the underlying therapeutic molecule and physiologic bases of the therapeutic effects of ADAMTS-13 polypeptide in the treatment of a patient positive for an anti-ADAMTS-13 antibody.

Reasonable correlation must exist between the scope of the claims and scope of the enablement set forth. In view on the quantity of experimentation necessary the limited working examples, the nature of the invention, the state of the prior art, the unpredictability of the art and the breadth of the claims, it would take undue trials and errors to practice the claimed invention.

16. Claims 1-4 and 8-13 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant is in possession of an isolated polypeptide of SEQ ID NO: 1, an isolated polypeptide consisting of amino acids 446-687 of SEQ ID NO: 1 and a composition thereof.

Applicant is not in possession of a polypeptide "comprising" any neutralizing epitope region in vWF-cp/ADAMTS-13 which is recognized by an antibody against the protease, or any peptide derived from the polypeptide in claim 1, or the polypeptide or the peptide fragment "derived from" said polypeptide, wherein the neutralizing epitope region is located in a region from position 449-687 in an amino acid sequence shown in SEQ ID NO: 1, in claim 2, or a polypeptide "comprising" an amino acid sequence from position 449-687 in an amino acid sequence shown in SEQ ID NO:1, or any peptide fragment "derived from" the polypeptide in claim 3, a polypeptide comprising an amino acid sequence consisting of an amino acid sequence from position 449-687 in an amino acid sequence shown in SEQ ID NO: 1. "where one of several amino acids are deleted, substituted, or added, the polypeptide being recognized by an antibody against vWF-cp, or a peptide fragment derived from the polypeptide" in claim 4, or a reagent for antibody measurement comprising a polypeptide "having a complete sequence composing ADAMTS-13, or a polypeptide or a peptide fragment derived from the polypeptide in claim 8, where in an autoantibody in a TTP patient is an object to be detected in claim 9; or a "pharmaceutical" composition for treating a patient positive for an anti-ADAMTS-13 antibody comprising, as an active ingredient, a polypeptide or a peptide fragment derived from the polypeptide in claim 10, or the pharmaceutical composition for treating a patient positive for an anti-ADAMTS-13 antibody, wherein the pharmaceutical composition comprises, as an active ingredient, a polypeptide or a peptide fragment derived from the polypeptide composed of a polypeptide or a polypeptide according to claims 1-4m, which lacks reactivity with an anti-ADAMTS-13 antibody by modification such as molecular substitution, deletion or insertion in claim 11, wherein the pharmaceutical composition is administered to the patient to thereby neutralize the antibody in claim 12, or a composition comprising a ligand specific to an anti-ADAMTS-13 antibody for treating a patient positive for an anti-ANDAMTS-13 antibody, comprising , as an active ingredient, a polypeptide or a peptide fragment derived from the polypeptide according to claim s1-4, which is bound with a carrier and brought into contact with plasma from the patient to be used for removing the anti-ADAMT fragment antibody from the plasma from the patient in claim 13.

Applicant has disclosed only amino acid of SEQ ID NO: 1 and polypeptides comprising aa449-687 of SEQ ID NO: 1; therefore, the skilled artisan cannot envision all the contemplated amino acid sequence possibilities recited in the instant claims. Consequently, conception cannot be achieved until a representative description of the structural and functional properties of the claimed invention has occurred, regardless of the complexity or simplicity of the method. Adequate written description requires more than a mere statement that it is part of the invention. See *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (CAFC1993). The Guidelines for the Examination of Patent Application Under the 35 U.S.C.112, ¶ 1"Written Description" Requirement make clear that the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species disclosure of relevant, identifying characteristics, i.e., structure or other physical and or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the genus (Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 20001, see especially page 1106 3rd column).

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the written description inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.). Consequently, Applicant was not in possession of the instant claimed invention. See University of California v. Eli Lilly and Co. 43 USPQ2d 1398.

Applicant is directed to the final Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

17. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

18. Claims 1-4 and 8-13 are rejected under 35 U.S.C. 102(a) as being anticipated by Soejima *et al* (Blood, Epub 7/17/2003, pages 1-36).

Soejima *et al* teach ADAMTS-13 cysteine-rich/spacer domains are functionally essential for vWF cleavage. Furthermore, Soejima et al teach 13 sequential COOH-terminal truncated mutants and a single-pont mutant (RGD to RGE in the cystein-rich domain), and compared the activity of each mutant with that of the wild-type protein. Soejima et al also performed epitope

mapping of autoantibodies against ADAMTS-13 and found that the major epitopes of these antibodies were found to reside within the cysteine-rich/spacer domains. Soejima et al concluded that the ADAMTS-13 cysteine-rich/spacer domains (i.e., aa 449-687 of SEQ ID NO: 1) are essential for VWF-CP activity (see Abstract, page 9, under *Epitope Mapping...*, Figure 1, W688X). Finally, Soejima et al teach the wild-type and the W688X mutant protein were in culture media (pharmaceutical composition) (see pages 9 and 13, under *Epitope Mapping...* in particular).

The reference teachings anticipate the claimed invention.

19. Claims 1-4 and 8-13 are rejected under 35 U.S.C. 102(a) as being anticipated by Plaimauer et al (IDS ref. A3).

Plaimauer et al teach cloned ADAMTS-13 fragments like cysteine-rich/spacer region (claimed polypeptide consisting of 449-687). Plaimauer et al teach that the fragments were isolated from inclusion bodies and purified by Ni-IMAC and subsequent IEX-chromatography under denatureing conditions. Plaimauer et al teach that analyses are still ongoing and data from the first analyzed TTP plasmas imply that major epitopes are recognized in the catalytic/distintegrin/TSP1, the cysteine-rich/spacer and the CUB domains emphasizing their functional importance for ADAMTS-13 activity. Plaimauer et al further teach the full-length ADAMTS-13 which comprises the neutralizing epitope region aa 449-687 of the ADAMTS-13.

The recitation that the polypeptide is "recognized by an antibody against the protease" is considered inherent properties of the referenced polypeptide. That is the antibody would bind said fragments.

Claims 8-13 are included because the purified cysteine-rich/spacer region must be in a composition formulation. Further, in order for the analyses of the ADAMTS-13 fragments activities, the fragments must be in the composition formulation.

The intended uses and the claimed functional limitations do not carry patentable weight per se and the claims read on the active or essential ingredients of the polypeptide.

The reference teachings anticipate the claimed invention.

20. Claims 1-4 and 8-13 are rejected under 35 U.S.C. 102(a) as being anticipated by Zheng et al (J Biol Chem. 2003 Aug 8;278(32):30136-41. Epub 2003 Jun 5).

Zheng et al teach several ADAMTS13 constructs such as FL, del1 and del2 which comprises the Cys-rich/spacer region. Zheng et al further teach del3 construct that comprises the spacer "a peptide fragemtn derived from the polypeptide comprising aa 449-687) (see Fig. 1 in particular). Claim 4 is included because the claim recites one or several amino acids are added, that would open up the claim to included the extra amino acids taught by the Zheng et al reference. Further,

Zheng et al specifically teach that the spacer domain (fragment of the polypeptide) is required to recognize and cleave VWF (see page 30136 last ¶ in particular). Further, deletion of the spacer domain in construct del3 abolished activity (see page 30139, 2nd col., top ¶ in particular). Finally, Zheng et al teach the recombinant ADAMTS13 in (5 µl) conditioned medium, which is considered to be pharmaceutical acceptable carrier. The intended uses and the claimed functional limitations do not carry patentable weight per se and the claims read on the active or essential ingredients of the polypeptide.

The recitation that the polypeptide is "recognized by an antibody against the protease" is considered inherent properties of the referenced polypeptide. That is the antibody would bind said fragments.

The reference teachings anticipate the claimed invention

21. Claims 1-4 and 8-13 are rejected under 35 U.S.C. 102(b) as being anticipated by Zheng *et al* (Bood, (November 16, 2002) Vol. 100, No. 11, Abstract No. 974.

Zheng *et al* teach both wild-type as well as C-terminal truncated forms of ADAMTS-13 proteins. Zheng *et al* teach that Wild-type recombinant ADAMTS13 appeared to localized to the cytoplasm, plasma membrane and extracellular matrix. Truncation after the first TSP-1 motif (comprising amino acids 449-687 of SEQ ID NO:1) abolished the extracellular matrix localization, suggesting that the extracellular Matrix proteins may interact with the thrombospondin type 1 motifs, cystiene rich domain, or spacer region of ADAMTS13. Zheng *et al* teach that the activity of recombinant ADAMTS13 was metal dependent and was inhibited by immunoglobulin G autoantibody isolated from idiopathic TTP patients. Zheng *et al* teach that the isolated metalloprotease domain of ADAMTS13 was not able to cleave von Willebrand factor, nor were constructs truncated after the disintegrin domain, the first TSP1 motif (comprising amino acids 449-687 of SEQ ID NO:1) or the cysteine rich domain (i.e., peptide fragment derived from the polypeptide). Zheng et al teach that addition of the spacer region restored at least 50% of protease activity and the further addition of the remaining seven thrombospondin type 1 motifs restored the protease activity to approximately 80% of the wild-type ADAMTS13 protein. Zheng et al concluded that the spacer region, additional seven TSP-1 motifs and two CUB domains may contribute to full metalloprotease activity toward vWF (see abstract).

The recitation that the polypeptide is "recognized by an antibody against the protease" is considered inherent properties of the referenced polypeptide. That is the antibody would bind said fragments.

Claims 8-13 are included because in order to perform the ADAMTS13 activities, ADAMTS13 must be in a composition formulation. Further, the intended uses and the claimed functional limitations do not carry patentable weight per se and the claims read on the active or essential ingredients of the polypeptide.
The reference teachings anticipate the claimed invention.

22. Claims 1-4 and 8-13 are rejected under 35 U.S.C. 102(b) as being anticipated by Soejima et al (IDS Ref. B3).

Soejima et al teach a novel human metalloprotease synthesized in the liver and secreted into the blood: Possibly, the vWF-cp (see Fig 1A). The reference vWF-cp comprises an amino acid sequence from postion 449 to position 687 in an amino acid sequence shown in SEQ ID NO: 1. Soejima et al teach purification of vWF-cp, where in the precipitated active fraction was dissolved in buffer B. Buffer B is considered a pharmaceutical active carrier. The intended uses and the claimed functional limitations do not carry patentable weight per se and the claims read on the active or essential ingredients of the polypeptide.

The recitation that the polypeptide is "recognized by an antibody against the protease" is considered inherent properties of the referenced polypeptide. That is the antibody would bind said fragments.

The terms "derived from", "comprising" and "having" in claims 2-3 and 8 are open-ended, they would open up the polypeptide to include the referenced polypeptide. Claim 4 is included because the term "where one or several amino acids are added" would open up the polypeptide to include the vWF-cp.

The reference teachings anticipate the claimed invention.

22. Claims 1-4 are rejected under 35 U.S.C. 102(b) as being anticipated by Zheng et al (J Biol Chem. 2001 Nov 2;276(44):41059-63. IDS Ref C1).

Zheng et al teach VWFCP consists of 1427 amino acid residues comprising Cys-rich domain and ADAMTS spacer (aa449-687 of SEQ ID NO:1) (see abstract and Fig. 1 and Fig. 2 in particular). Zheng et al teach delineate the Cys-rich and the ADAMTS spacer (a specific fragment of aa449-687 of SEQ ID NO:1. Further Zheng et al teach a fragment consisting of RGDS. A fragment consisting of Cys-rich domain contains an RGDS sequence that could mediate integrin-dependent binding to platelets or other cells. Furthermore, Zheng et al teaches alternative splicing gives rise to at least seven potential variants that trucncate the protein at different positions after the protease domain. Alternative splicing may have functional significance, producing proteins with distinct abilities to interact with cofactors, connective tissue, platelets and VWF (see abstract in particular). These insertions and deletions cause frameshifts and truncation after the metalloprotease domain, the spacer domain or the first CUB domain (each results in two fragments, one fragment comprises the Cys-rich/spacer) or cause an in-frame deletion of 56 amino acids between the eighth TSP1 domain and the first CUB domain (see page 41062, 1st col., 1st ¶ in particular).

The reference teachings anticipate the claimed invention.

23. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

24. Claims 1-4 and 8-13 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 30-32 of copending Application No. 10/529,009. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claims are expressly claiming the same subject mater, although they differ in scope. Specifically, pending claims 30-32 of the `009 application and instant claims are directed to a polypeptide or a peptide fragment derived from the ADAMTS-13 polypeptide.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

25. No claim is allowed.

26. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maher Haddad whose telephone number is (571) 272-0845. The examiner can normally be reached Monday through Friday from 7:30 am to 4:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841. The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

January 3, 2008

Maher Haddad

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